IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., AND SHIRE US INC., Plaintiffs, v. BARR LABORATORIES, INC., Defendant.	09 Civ. 2380 (PGG) (KNF)
SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., AND SHIRE US INC., Plaintiffs, v. MYLAN INC., MYLAN PHARMACEUTICALS INC., AND MATRIX LABORATORIES LIMITED, Defendants.	09 Civ. 2555 (PGG) (KNF)
SHIRE CANADA INC., SHIRE INTERNATIONAL LICENSING B.V., AND SHIRE US INC., Plaintiffs, v. NATCO PHARMA LIMITED, Defendant.	09 Civ. 3165 (PGG) (KNF) ECF CASE

PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

CASES

I. INTRODUCTION

This case concerns the efforts of three generic drug manufacturers to obtain approval from the Food and Drug Administration to manufacture and sell generic versions of Fosrenol®, a novel treatment for the medical condition hyperphosphatemia. Fosrenol® was developed by Plaintiffs (collectively, "Shire") through nearly a decade of research and testing. It was the first, and is the only, drug approved by the FDA whose active ingredient is lanthanum, a rare earth metal, and was awarded "New Chemical Entity" exclusivity by the FDA upon approval. After the safety and efficacy of Fosrenol® were established, and now that Fosrenol® has proven successful, Defendants seek to obtain approval for generic versions of it.

Shire owns three patents directed to the treatment of hyperphosphatemia using lanthanum carbonate – U.S. Patent No. 5,968,976 (the '976 Patent), U.S. Patent No. 7,465,465 (the '465 Patent), and U.S. Patent No. 7,381,428 (the '428 Patent). Hyperphosphatemia is a condition characterized by excess levels of phosphate in the blood. *See, e.g.,* JA 0006 ('976 Patent, Col. 1:11-16). Elevated phosphate levels can cause serious harm to a patient, such as calcification of soft tissue, hypocalcemia, and increased risk of cardiovascular disease. *See* Declaration of Paul J. Scheel, M.D. ("Scheel Decl.") ¶ 9. Hyperphosphatemia is common in patients suffering from chronic kidney disease because phosphate is found in food and absorbed as people eat. In a healthy individual, the kidneys regulate the level of phosphate in the blood to maintain a substantially constant and safe level. But when patients suffer from kidney failure such as in end-stage renal disease, the body's regulation mechanism stops working properly resulting in an increasing level of phosphate in the blood. Further, dialysis fails to remove phosphate from the blood sufficiently to prevent an increase in blood phosphate levels over time. *See id.* ¶¶ 8-10.

To treat hyperphosphatemia, doctors have long prescribed pharmaceutical compositions containing elements that bind to phosphate. Such bound phosphate is excreted from the body

rather than absorbed. *See* Scheel Decl. ¶¶ 10-11. Shire's patents concern the discovery of a novel treatment for hyperphosphatemia using lanthanum carbonate, which overcomes problems with prior phosphate binding drugs. Prior to the inventions of the '976 Patent, two types of compositions were prescribed as phosphate binders: (1) aluminum compounds such as aluminum hydroxide and (2) calcium compounds such as calcium carbonate. *See* JA 0006 ('976 Patent, Col. 1:14-19). Aluminum was found to have toxic effects on patients. *See id.* (Col. 1:16-17); Scheel Decl. ¶ 12. The calcium in calcium compounds was found to be absorbed readily in the gut in addition to binding to phosphate, causing patients to suffer from too much calcium in the blood, *i.e.*, hypercalcemia. *See* JA 0006 ('976 Patent, Col. 1:17-19); Scheel Decl. ¶ 13.

Recognizing the need for improved hyperphosphatemia treatments, scientists at Johnson Matthey PLC, with support from Shire, initiated a multi-year research project in 1991 to investigate the possible use of "rare earth metal" compounds as treatments for hyperphosphatemia. Rare earth metals are a class of elements including lanthanum, cerium, praseodymium, samarium, ytterbium, and gadolinium. Through an investigation and assessment of a large number of rare earth metal compounds, Johnson Matthey and Shire identified lanthanum carbonate as a promising phosphate binder.

The inventors of the '976 Patent, Dr. Barry Murrer and Dr. Nigel Powell, then discovered that particular crystalline forms of lanthanum carbonate showed the greatest phosphate binding in *in vitro* testing intended to simulate conditions in the gastrointestinal system. They further showed through *in vivo* studies that these lanthanum carbonate hydrates should be safe for administration to patients.

Significant difficulties remained in designing a drug to administer this active ingredient to patients suffering from hyperphosphatemia. The inventors of the '465 Patent discovered ways

to formulate and manufacture lanthanum carbonate hydrates in chewable tablets that can be easily taken with meals (where phosphate enters the gastrointestinal system), with little or no fluid. Limiting fluid intake is a key aspect of treating patients with end stage renal disease, whose kidneys often cannot process fluids properly. Yet achieving a chewable formulation was difficult. For example, lanthanum carbonate proved difficult to form into tablets. The very large amounts of lanthanum carbonate in each tablet necessary to provide the required dose of elemental lanthanum made development of manufacturing processes challenging, especially since the tablets needed to be hard enough to survive both the manufacturing process and storage in bottles but soft enough to be easily chewable. The inventors ultimately succeeded in identifying ingredients and process steps to make chewable tablets of lanthanum carbonate hydrates suitable for treating hyperphosphatemia.

It was found that lanthanum carbonate hydrates degrade in the presence of heat and humidity to form the compound lanthanum hydroxycarbonate. The inventors of the '428 Patent discovered that including monosaccharides or disaccharides – particular types of inactive ingredients – in sufficient amounts in lanthanum carbonate formulations significantly retarded or prevented this degradation to lanthanum hydroxycarbonate. This stabilization of the formulation was significant because FDA requirements limit the amount of such degradation in drug products.

II. THE LAW OF CLAIM CONSTRUCTION

A court "look[s] to the words of the claims themselves . . . to define the scope of the patented invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (*en banc*) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). A claim term is generally given its "ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention."

Id. at 1313. Thus, "the court looks to 'those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean,' . . . . includ[ing] 'the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.'" *Id.* at 1314 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

The "specification is always highly relevant to the claim construction analysis" and serves as "the single best guide to the meaning of a disputed term." *Vitronics Corp.*, 90 F.3d at 1582; *see also Phillips*, 415 F.3d at 1311-12. "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. But a patentee who chooses to act as his own lexicographer must "clearly define terms used in the claims in the specification." *Sinorgchem Co. v. Int'l Trade Comm'n*, 511 F.3d 1132, 1136 (Fed. Cir. 2007). The Federal Circuit has also cautioned that when consulting the specification, a court must take care not to import limitations into the claims from the specification. *Voda v. Cordis Corp.*, 536 F.3d 1311, 1320 (Fed. Cir. 2008); *see Phillips*, 415 F.3d at 1323.

In addition to the specification, a court should consider the patent's prosecution history. *See, e.g.*, *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*; *see also id.* ("Like the specification, the prosecution history provides evidence of how the [Patent Office] and the inventor understood the patent.").

Extrinsic evidence such as expert testimony and dictionaries may also be considered to obtain a reliable interpretation of a claim limitation. *See, e.g.*, *Boston Scientific Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 985-87 (Fed. Cir. 2009). Indeed, "dictionaries and treatises can be useful in claim construction." *Phillips*, 415 F.3d at 1318. Courts have "especially noted the help that technical dictionaries may provide . . . to better understand the underlying technology and the way in which one of skill in the art might use the claim terms." *Id.* (internal quotation marks omitted); *see also id.* at 314. Extrinsic evidence, however, is considered "less significant than the intrinsic record" in construing claims. *Id.* at 1317.

A proper claim construction should align with the problem in the existing art, the objective of the invention, and the stated benefit of the invention. *See CVI/Beta Ventures v. Tura LP*, 112 F.3d 1146, 1160 (Fed. Cir. 1997) (problem inventor was attempting to solve); *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1251-52 (Fed. Cir. 1998) (purpose of the invention); *Laitram Corp. v. Morehouse Indus.*, 143 F.3d 1456, 1463 (Fed. Cir. 1998) (stated benefits of the invention).

III. CONSTRUCTION OF TERMS OF U.S. PATENT NO. 5,968,976

The claims of the '976 Patent use terminology having clear and well-understood meanings to persons of skill in the art. Thus, the claim construction task for these claims ought to be straightforward. The intrinsic evidence demonstrates that the patentees used terms according to their plain and ordinary meanings.

Defendants advance claim constructions that ignore the claim language and intrinsic record and improperly seek to introduce limitations into the claims unsupported by their language and at odds with the '976 Patent's written description. Most egregiously, they repeatedly attempt to rewrite the claims to add two types of limitations. First, they propose to add a "quantity" limitation – that the compositions must have a certain amount of the claimed

lanthanum carbonate hydrates – where none is warranted or even hinted at in the claims. *See infra* Section III.A. Second, they propose to transmute claims directed to crystalline forms of lanthanum carbonate into claims concerning an amount of water in a bulk composition (regardless of crystal structure). *See infra* Section III.B. In so doing, they advance constructions inconsistent with the very inventions taught in the patents. Defendants pursue these claim constructions simply to generate noninfringement positions. These unsupported claim constructions should be rejected.

A. "pharmaceutical composition for the treatment of hyperphosphatemia" (Claim 1)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
pharmaceutical composition for the treatment of hyperphosphatemia	therapeutic mixture (*i.e.*, one which is sterile, reasonably safe and non-toxic) suitable for administration into the gastrointestinal tract for the treatment of hyperphosphatemia	a pharmaceutical composition wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphatemia

"Pharmaceutical composition" is a familiar term in the art, whose plain meaning is a mixture suitable for its intended therapeutic use, here the treatment of hyperphosphatemia. *See* Scheel Decl. ¶ 22; *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 579 F. Supp. 2d 199, 205 (D. Mass. 2008) (construing "pharmaceutical composition" to mean "suitable for administration to humans"); *Genentech, Inc. v. Boehringer Mannheim GmbH*, 989 F. Supp. 359, 368 (D. Mass. 1997) (construing "pharmaceutical compositions" to be those that are, among other things, "acceptable in their own right for administration to humans").

Rather than interpret the term, Defendants attempt to rewrite it, adding a quantity limitation not present in claim 1: "the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition . . . effective to." Defendants make up this limitation out of whole cloth in a transparent attempt to fashion a noninfringement argument. Claim 1 makes clear that it is the composition as whole

that is suitable for the treatment of hyperphosphatemia. The claim does not include a limitation on the amount of any particular crystalline form present in the composition. Rather, the claim is written as an "open" claim: The claim recites "[a] pharmaceutical composition for the treatment of hyperphosphataemia *comprising*," and the Federal Circuit has explained that "[i]n the patent claim context the term 'comprising' is well understood to mean 'including but not limited to.'" *CIAS, Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007); *KIS, S.A. v. Foto Fantasy, Inc.*, 60 Fed. Appx. 319, 323 n.3 (Fed. Cir. 2003) ("Because claim 1 was drafted using the recognized term of art 'comprising' in the transitional language, it is an 'open' claim that must be construed as including the recited elements, but not excluding additional, unrecited elements.").

Defendants further disregard that when the inventors wanted to claim an amount of lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ effective to treat hyperphosphatemia, they did so expressly, as they did in claim 7. *See* JA 0008 ('976 Patent, Col. 6:39-47).

That Defendants are not clarifying any ambiguous claim language is readily apparent; they leave the actual language from the claim virtually unchanged. Yet it was Defendants that identified this claim term as requiring construction. Defendants' attempt to use claim construction proceedings to narrow claim 1 should be rejected.

Because Defendants identified the term as requiring construction, however, Shire has sought to bring greater clarity to it. While the applicants made clear during the prosecution of the '976 Patent that they used "pharmaceutical composition" consistent with its plain meaning, they elucidated certain aspects of it. Thus, in responding to a rejection by the patent Examiner, the applicants explained that a "pharmaceutical composition" must be one "considered suitable for administration to a patient." JA 0242 (11/19/98 Remarks at 7). They stated that a

pharmaceutical composition must be sterile and free from toxic ingredients. *See* JA 0243; JA 0241. Additionally, because claim 1 recites that the composition is "in a form for administration to the gastrointestinal tract," it follows that the "pharmaceutical composition" must be suitable for such administration. *See also* JA 0006 ('976 Patent, Col. 1:59-63); JA 0008 (Col. 5:8-11).

Thus, in light of the prosecution history and the ordinary meaning of the term, "pharmaceutical composition" should be construed to mean **"therapeutic mixture (*i.e.*, one which is sterile, reasonably safe and non-toxic) suitable for administration into the gastrointestinal tract for the treatment of hyperphosphatemia."**

B. "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ wherein x has a value from" (Claims 1, 7)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ wherein x has a value from	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate, wherein x has a value from	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from

The term "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$" has a plain and ordinary meaning to persons of skill in the art of the '976 Patent. It refers to a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate. *See* Declaration of Allan Myerson, Ph.D. ("Myerson Decl.") ¶¶ 41-42. As set forth below, this construction is supported by both the specification and the prosecution history. Defendants, however, attempt to generate non-infringement arguments by proposing that the term be construed in a manner at odds with its plain and ordinary meaning. According to Defendants, the term refers not to any crystalline structure but to the distinct concept of an "average water content" in a bulk composition. This outcome-driven proposed construction lacks merit and should be rejected.

When the claims, specification, and prosecution history are read from the perspective of a person of ordinary skill, as they must be, the conclusion necessarily follows that the chemical formula is used in accordance with its plain and ordinary meaning. To assist the Court in understanding the chemical formula and the intrinsic evidence supporting its proper construction, Shire first provides a brief background on the technology of hydrates (of which the claimed lanthanum carbonate hydrates are examples). *See* JA 0001 ('976 Abstract) (explaining that "[s]elected lanthanum carbonate hydrates may be administered . . . to treat hyperphosphataemia").

1. Background on Hydrates.

A "hydrate" is a type of crystal. *See* Myerson Decl. ¶ 25; *id.* ¶ 21 (providing pictures of two hydrates). Crystals are solids in which the constituent units (here, compounds) are chemically bonded and arranged in a periodic repeating pattern that extends in three dimensions. *See id.* ¶ 16. This pattern can be described by a "unit cell," the smallest repeating structure in the crystal, which can be used to distinguish one crystalline form from another. *See id.* ¶ 21. The regular pattern of the crystal's constituent units is referred to as the "crystalline lattice." *See id.* ¶ 18.

Hydrates are chemical species whose crystal structure contains water molecules bonded as part of the crystal lattice. *See, e.g.*, JA 6003 (STEDMAN'S MEDICAL DICTIONARY 814 (26th ed. 1995)) (defining "hydrate" as "a compound crystallizing with one or more molecules of water; *e.g.*, $CuSO_4 \cdot 5H_2O$"); JA 6009 (HANDBOOK OF INDUSTRIAL CRYSTALLIZATION 2 (Myerson ed., Butterworth-Heinemann 1st ed. 1993)) (a hydrate is "a solid formed upon crystallization from water that contains water molecules as part of its crystal structure"); Myerson Decl. ¶ 42. In a hydrate, the water "trapped" in the crystal lattice bonds with the other molecules or compounds of the crystal to form an altered crystalline structure. *See* Myerson Decl. ¶ 26.

The notation used to identify a hydrate is a chemical formula containing a dot followed "xH_2O," where x is a value signifying the number of moles of water for each mole of the molecule or compound. *See*, *e.g.*, Myerson Decl. ¶¶ 25, 41-42; JA 6009 (HANDBOOK OF INDUSTRIAL CRYSTALLIZATION 2) ("The chemical formula of a hydrate indicates the number of moles of water present per mole of the solute species by listing a stoichiometric number and water after the dot in the chemical formula."). (A "mole" is a standard unit for the amount of a substance, referring to 6.02×10^{23} units of the substance; thus, a mole of water is 6.02×10^{23} molecules of water. *See* Myerson Decl. ¶ 40 n.1.) For example, $CuSO_4\cdot5H_2O$ refers to copper sulfate pentahydrate, a hydrate of copper sulfate having five moles of water bound in the crystalline solid for each mole of copper (Cu) sulfate (SO_4).[1]

The number of moles of water bound in the crystal lattice – that is, the variable "x" – may also be referred to as the "waters of crystallization" or "waters of hydration."[2] *See, e.g.*, JA 6006 (STEDMAN'S MEDICAL DICTIONARY 1957) (defining "w[ater] of crystallization" as "w[ater] of constitution that unites with certain salts and is essential to their arrangement in crystalline form; *e.g.*, $CuSO_4\cdot5H_2O$"); *see generally Novartis Corp. v. Ben Venue Labs., Inc.*, 271 F.3d 1043, 1045 (Fed. Cir. 2001) (explaining that "pamidronate disodium pentahydrate [is] a crystalline material in which each molecule of pamidronate disodium occupies a defined position in a crystal lattice and is complexed with five water molecules" and that "[t]he water molecules bound to the

[1] In practice, crystals often have imperfections, such as defects (*e.g.*, foreign atoms in the crystal lattice) and vacancies (the absence of an atom from a lattice site). Myerson Decl. ¶ 28. Thus, crystals of a hydrate may have a non-integer ratio of water molecules to units of the compound even where "x" would have an integer value in a perfect crystal. Myerson Decl. ¶¶ 27, 51.

[2] The same ratio may be expressed as the number of molecules of water per unit of the molecule or compound. *See, e.g.*, JA 0006-7 ('976 Patent, Col. 2:9-124, 3:43-46).

pamidronate disodium in the crystal are termed the water of crystallization."); Myerson Decl. ¶ 26. Thus, $CuSO_4 \cdot 5H_2O$ may be described as having five waters of crystallization or five waters of hydration.

A chemical species may have multiple hydrates. *See id.* This means a given compound might be made to form crystals having different numbers of water molecules bonded as part of the crystal lattice. *See id.* Each of these hydrates will have a different crystal structure owing to the different number of water molecules bound as part of the lattice. Lanthanum carbonate is illustrative. Lanthanum carbonate is a compound of lanthanum (La) and carbonate (CO_3), whose chemical formula is $La_2(CO_3)_3$. Chemistry literature cited in the prosecution of the '976 Patent identified five different lanthanum carbonate hydrates. *See* JA 0187 (9/11/98 Office Action at 5) (citing "$La_2(CO_3)_3 \cdot nH_2O$ where the variable of n is equal to 1, 3, 5, and 8" in the Oda reference, $La_2(CO_3)_3 \cdot 3H_2O$ in Mineely et al. reference, $La_2(CO_3)_3 \cdot 5H_2O$ in the Yanagihara et al. reference, and $La_2(CO_3)_3 \cdot 6H_2O$ in the Mzareulishvili reference). The "[s]elected lanthanum hydrates" of the '976 Patent, in which "x" is between 3 and 6, are crystalline forms of lanthanum carbonate with 3 to 6 water molecules bonded as part of their crystal lattices per unit of lanthanum carbonate.

Different hydrates of a chemical species may have significantly different physical properties, such as hardness, solubility, and dissolution rate. *See* Myerson Decl. ¶ 23.

2. "$La_2(CO_3)_3 \cdot xH_2O$" Has a Plain and Ordinary Meaning.

A claim term is generally given its "ordinary and customary meaning." *Phillips*, 415 F.3d at 1313. Here, the formula "$La_2(CO_3)_3 \cdot xH_2O$" has an ordinary and customary meaning. Both the chemical symbols for lanthanum carbonate, $La_2(CO_3)_3$, and the notation "$\cdot xH_2O$" were well-known and unambiguous at the time of the invention. Together, they refer to a crystalline

form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate. *See* Myerson Decl. ¶¶ 41-42; *see also id.* ¶¶ 25-26.

As described above, the notation "·xH_2O" used in the chemical formula was and is standard notation for hydrates, with "x" acting as a variable for the number of moles of water per mole of the compound. The prosecution history illustrates how conventional this notation is. The Examiner at one point rejected the claims on the ground that several general chemistry references disclosed the existence of lanthanum carbonate of the claimed formula because they, respectively, "teach[] of $La_2(CO_3)_3 \cdot nH_2O$ where the variable n is equal to 1, 3, 5, and 8" (Oda abstract), "teach of $La_2(CO_3)_3 \cdot 3H_2O$" (Mineely et al. abstract), and "teach of $La_2(CO_3)_3 \cdot 6H_2O$" (Mzareulishvili et al. abstract). *See* JA 0187-0190 (9/4/1998 Office Action at 5-8). Certain of these references explicitly state that this formula refers to a hydrate. *See* JA 0194 (Mineely et al. abstract) (disclosing "$La_2(CO_3)_3 \cdot 3H_2O$" and referring to it as "Lanthanum carbonate ($La_2(CO_3)_3$ *trihydrate*") (emphasis added); JA 00201-0203 (Yanagihara et al. at 226-228) (disclosing "$La_2(CO_3)_3 \cdot 5H_2O$" and explaining that "[l]anthanum carbonate was isolated as the *pentahydrate*") (emphasis added). The Oda reference's title is also instructive: "Studies on the *crystal water* of lanthanum carbonate." JA 0197 (emphasis added). Thus, the prosecution history indicates that both the Examiner and applicants understood $La_2(CO_3)_3 \cdot xH_2O$ to refer, as it ordinarily does, to hydrate forms of lanthanum carbonate. And in successfully overcoming the Examiner's anticipation rejections based on these chemistry references, the applicants never suggested that they used the formula $La_2(CO_3)_3 \cdot xH_2O$ in a manner different than its well-accepted meaning.

3. The Intrinsic Evidence Demonstrates That the Inventors Used the Term "$La_2(CO_3)_3 \cdot xH_2O$" According to Its Ordinary and Customary Meaning.

The intrinsic evidence – the other claims, the specification, and the prosecution history – demonstrate that $La_2(CO_3)_3 \cdot xH_2O$ has its customary meaning in the '976 Patent.

Claim 5 conveys that "$La_2(CO_3)_3 \cdot xH_2O$ where x has a value from 3 to 6" is lanthanum carbonate "with 3 to 6 molecules of water of crystallization." JA 0008. As explained above, "water of crystallization" had a well-defined meaning, referring to the number of moles or molecules of water bound as part of the crystal structure. *See supra* Section III.B; *see also* Myerson Decl. ¶ 46. It is well established that "[o]ther claims of the patent in question, both asserted and unasserted, can . . . be valuable sources of enlightenment as to the meaning of a claim term." *Phillips*, 415 F.3d at 1314. Here, claim 5 recites "[a] process for the preparation of lanthanum carbonate *as defined in any one of claims 1 to 3*" (emphasis added), *i.e.*, a process yielding $La_2(CO_3)_3 \cdot xH_2O$ where x is between 3 and 6. The final step of claim 5, to obtain the lanthanum carbonate hydrates of claims 1-3, is to dry lanthanum carbonate octahydrate "so as to obtain a lanthanum carbonate *with 3 to 6 molecules of water of crystallisation*" (emphasis added). Claim 5 thus reinforces that the claimed formula refers to crystalline forms of lanthanum carbonate containing 3-6 moles of water as part of its crystal structure per mole of lanthanum carbonate.[3]

The specification and prosecution history further show that the formula "$La_2(CO_3)_3 \cdot xH_2O$" was used in accordance with its plain and ordinary meaning. First, the

[3] The specification similarly describes lanthanum carbonate of the invention as having "3 to 6 waters of crystallization." *See, e.g.*, JA 0006 ('976 Patent, Col. 2:9-12) (describing controlled drying of lanthanum carbonate octahydrate "to obtain a lanthanum carbonate with 3 to 6 molecules of water of crystallisation"); *see also* JA 0007 ('976 Patent, Col. 3:43-46) (explaining that Figure 1 shows "that the highest possible phosphate removal is obtained with lanthanum carbonates having 3 to 6 molecules of water").

specification expressly uses the formula to describe particular lanthanum carbonate hydrates. For example, in column 1, the patentees explain that "$La_2(CO_3)_3 \cdot H_2O$" is "the monohydrate." JA 0006 ('976 Patent, Col. 1:44-47). In the next paragraph, the specification refers to "the octahydrate form" of lanthanum carbonate. *Id.* (Col. 1:51).

Throughout the specification, the patentees refer to their invention as "[*s*]*elected* lanthanum carbonate *hydrates*," JA 0001 ('976 Patent, Abstract) (emphases added), "*certain* lanthanum carbonate *hydrates*," JA 0006 (Col. 2:61-64) (emphases added), and "*certain forms* of lanthanum carbonate," JA 0006 (Col. 1:48-52) (emphasis added). During prosecution, the applicants explained that "[t]he invention resides in the unexpected discovery that lanthanum carbonates with waters of crystallization or hydration between 3 and 6 moles of water per mole of lanthanum carbonate are particularly effective in absorbing phosphate both *in vivo* and *in vitro*." JA 212 (11/11/98 Amendment and Remarks at 3); JA 0238 (11/19/98 Amendment and Remarks at 3) (same). They noted that "there is nothing in the art which suggests the use of hydrates with this specific range for any pharmaceutical use whatsoever." JA 0243 (11/19/98 Amendment and Remarks at 8).

Second, the claims, specification, and prosecution history interchangeably refer to the inventions as "$La_2(CO_3)_3 \cdot xH_2O$ where x has a value from 3 to 6," "lanthanum carbonate with 3 to 6 molecules of water of crystallization," and "lanthanum carbonate with waters of hydration between 3 and 6." According to the plain meanings of these terms as well, the formula refers to crystalline forms of lanthanum carbonate containing 3-6 moles of water as part of its crystal structure per mole of lanthanum carbonate.

During prosecution, for example, the applicants consistently described their invention as "lanthanum carbonate with waters of hydration in the range of 3-6." JA 0212-0213 (11/11/98

Amendment and Remarks at 3-4).[4] The Examiner recognized that "the specification demonstrates that the claimed compounds have unexpected results over other hydrates of lanthanum carbonates outside the claimed range," including substantial phosphate binding by "[s]ample 6, which has 3.8 waters of hydration." JA 0251-0252 (1/28/99 Office Action at 3-4).

Third, the specification teaches that the invention relates to the crystalline form of lanthanum carbonate. A person of ordinary skill in the art would understand that different hydrates, owing to their differing crystal structures, could have different physical properties. Consistent with this, the specification contrasts observed differences in the phosphate binding of crystalline forms of lanthanum carbonate of the invention from that of two known forms, lanthanum carbonate monohydrate and lanthanum carbonate octahydrate: "We have now discovered that *certain forms* of lanthanum carbonate exhibit improved performance in a variety of tests, over standard commercial lanthanum carbonate, which is believed to be the octahydrate form, and over $La_2(CO_3)_3.H_2O$ [*i.e.*, the monohydrate] or similar compounds." JA 0006 ('976 Patent, Col. 1:48-52) (emphasis added). The comparison to the octahydrate form and the monohydrate form implies that the "certain forms" discovered – and claimed as "lanthanum carbonate of the formula $La_2(CO_3)_3.xH_2O$ where x has a value" between 3 and 6 – are themselves particular forms. *See also* JA 0006 ('976 Patent, Col. 2:61-64) (drawing a similar comparison in discussing testing "to show that *certain lanthanum carbonate hydrates* are significantly different in phosphate binding activity from both lanthanum carbonate octahydrate

[4] *See also* JA 0215 (11/11/98 Amendment and Remarks at 6) (explaining that "the claimed methods of the invention . . . utilize lanthanum carbonate hydrates having waters of hydration in the particular range 3-6 which are particularly effective at absorbing phosphate at low pH"); JA 0258 (4/8/99 Amendment and Remarks at 2) ("The present application shows that the claimed lanthanum carbonates with waters of hydration between 3 and 6 are superior in their ability to absorb phosphate quickly and completely.").

and from $La_2(CO_3)_3 \cdot H_2O$") (emphasis added). Moreover, the specification explains Figure 4 as showing that "lanthanum carbonate $8.8H_2O$ . . . has a different crystalline structure from lanthanum carbonate $4H_2O$." JA 0008 ('976 Patent, Col. 5:1-4); Myerson Decl. ¶ 51.

Defendants strain to advance a construction defining the chemical formula as something other than crystalline forms of lanthanum carbonate, proposing instead that it somehow means that "the lanthanum carbonate present in the composition has an *average water content* equivalent to" a certain ratio. Their proposed construction does not accord with the ordinary meaning of the claim term or the description of the inventions in the specification and prosecution history. "Average water content" was not a concept unknown at the time of the '976 Patent. *See, e.g.*, Myerson Decl. ¶ 52. But it is conspicuously absent from the specification and prosecution history. Defendants' proposed construction thus contradicts the '976 Patent's reference to the crystalline form of lanthanum carbonate. It improperly and erroneously recasts the claim as concerning a bulk property of the overall pharmaceutical composition (average water content) rather than the crystalline forms of lanthanum carbonate in the composition. Defendants' attempt to redraft the claims in an effort to generate a non-infringement argument should be rejected.

The term "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$," therefore, should be construed according to its ordinary and customary meaning to skilled artisans, as supported by the intrinsic evidence: "**a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate**."

C. "unit dosage form to provide from 0.1 to 20g/day" (Claim 4)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
unit dosage form to provide from 0.1 to 20g/day	a solid or liquid form used to administer a dose of between 0.1 and 20g/day of elemental lanthanum	one or more unit dosage forms to provide a total daily dose of from 0.1 to 20 g/day of $La_2(CO_3)_3 \cdot xH_2O$

Claim 4 depends from any of claims 1-3 and specifies the doses to be administered to a patient. The "unit dosage form" according to claim 4 can be in either solid or liquid form. *See* JA 0008 ('976 Patent, Col. 5:17-25) ("Suitable forms for oral administration include *solid forms* such as tablets, capsules and dragees and *liquid forms* such as suspensions or syrups." (emphases added)).

The principal difference between the parties' proposed constructions is whether 0.1 to 20 grams per day refers to grams of *elemental* lanthanum (*i.e.*, the weight of the lanthanum in the composition) or grams of the particular lanthanum carbonate hydrate used (*i.e.*, the combined weight of the lanthanum, carbonate, and water). The intrinsic evidence conclusively answers this question, making clear that the relevant unit for purposes of dosing is the weight of the elemental lanthanum.

First, the '976 Patent teaches that what actually "bind[s] phosphate in the gut" is elemental lanthanum, which binds with phosphate to form lanthanum phosphate. *See* JA 0008 ('976 Patent, Col. 5:30-33) (discussing "lanthanum phosphate formed after binding to phosphate in the gut"). Dosing is stated most naturally in terms of what is binding phosphate – elemental lanthanum.

Second, *in vitro* phosphate binding experiments reported in the '976 Patent (JA 0006-0007, Col. 2:61-3:42) to compare the phosphate binding of different lanthanum carbonate hydrates were performed by holding constant the proportion of *elemental lanthanum* to phosphate. When the inventors tested the different lanthanum carbonate hydrates, each hydrate

"as a dry powder was added in an amount *according to the molecular weight of the particular hydrate*, to give a two-fold molar excess of *lanthanum* over phosphate and stirred at room temperature." JA 0007 ('976 Patent, Col. 3:9-14 (emphases added)). Thus, the specification makes clear that testing did *not* use a constant proportion of the particular lanthanum carbonate hydrate ($La_2(CO_3)_3 \cdot xH_2O$) to phosphate. On the contrary, keeping the proportion of elemental lanthanum to phosphate constant required using different amounts of the particular lanthanum carbonate hydrate since they would have different amounts of water and therefore different molecular weights. Because these experiments were intended to simulate phosphate binding in a patient's body, they are highly relevant to this issue of how the dosing claimed would be understood. *See* Scheel Decl. ¶ 33. The use of a constant proportion of elemental lanthanum to phosphate in the phosphate binding studies indicates that dosing according to the inventions is based on the amount of elemental lanthanum.

Third, prior art calcium-based phosphate binders referenced in the specification were typically dosed based on the amount of elemental calcium present in a tablet. The specification contrasts the "suitable daily dosage" of the claimed inventions to that known for a "commercial calcium-based phosphate binding composition." JA 0008 ('976 Patent, Col. 5:25-30); *see also id.* (Col. 5:13-15). Commercial calcium-based phosphate binders were dosed according to the amount of elemental calcium. *See* Scheel Decl. ¶ 32.

Shire's proposed construction of dosing based on the amount of elemental lanthanum is consistent with how a person of ordinary skill in the art would understand claim 4. As explained by Shire's expert nephrologist, Dr. Paul Scheel, a person of ordinary skill in the art at the time of

the invention would naturally understand the reference to dosing to refer to the weight of elemental lanthanum present in the composition. Scheel Decl. ¶¶ 30-33.[5]

Defendants, however, proposed to construe the term as "one or more unit dosage forms to provide a total daily dose of from 0.1 to 20 g/day of $La_2(CO_3)_3 \cdot xH_2O$." This construction is not supported by the intrinsic evidence, which points to the amount of elemental lanthanum as the unit measure for dosing, and is contrary to how a person of ordinary skill would understand the claim language.

Thus, the term "unit dosage form to provide from 0.1 to 20g/day" should be construed to mean **"a solid or liquid form used to administer a dose of between 0.1 and 20g/day of elemental lanthanum."**

D. "effective to treat said hyperphosphataemia" (Claim 7)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
effective to treat said hyperphosphataemia	capable, without toxic effects, of maintaining the serum phosphate level of a subject at a substantially constant level or reducing the serum phosphate level in a subject who has an excess level of serum phosphate	wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ p is effective to treat hyperphosphataemia

As explained above, hyperphosphatemia is a condition characterized by a rising level of phosphate in the blood. *See supra* Section I; *see also* JA 0006 ('976 Patent, Col. 1:11-14); Scheel Decl. ¶¶ 8-9. The specification states that in the context of the '976 Patent, "the term

[5] Shire's proposed construction is also consistent with how the '428 and '465 Patents refer to dosing of lanthanum carbonate hydrates. *See* JA 0044 ('428 Patent, Col. 10:42-25) ("The lanthanum carbonate formulation can be orally administered . . . in dosage forms varying from about 125 to about 2000 mg lanthanum carbonate as elemental lanthanum per meal."); JA 0016 ('465 Patent, Col. 6:57-60) (discussing "a pharmaceutical formulation in a tablet containing an amount of elemental lanthanum selected from 250 mg, 500 mg, 750 mg and 1000 mg").

'treatment' is intended to include preventative treatment." JA 0007 ('976 patent, Col. 3:52-53); Scheel Decl. ¶ 35. Thus "treatment" refers to maintaining the serum phosphate level of a subject at a substantially constant level or reducing the serum phosphate level in a subject who has an excess level of serum phosphate. *See* Scheel Decl. ¶¶ 34-35.

To be "effective to treat hyperphosphatemia," a composition must avoid causing toxic effects. Thus, the '976 Patent describes *in vivo* testing to demonstrate that lanthanum carbonate can treat hyperphosphatemia without toxic effects. *See* JA 0008 ('976 Patent, Col. 5:30-6:6). The specification explains that the inventions of the '976 Patent "offer[] the possibility of binding phosphate without any incursion of lanthanum into the blood stream, where toxic effects can cause problems." JA 0007 ('976 Patent, Col. 3:47-49).

Defendants' proposed construction, "wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ is effective to treat hyperphosphataemia," once again fails to define the claim language at issue ("effective to treat hyperphosphatemia"). Instead, Defendants attempt to insert a limitation before the claim language purportedly being construed, leaving the language from the claim unchanged as part of their proposed construction.

Based on its ordinary meaning as supported by the specification, "effective to treat said hyperphosphatemia" should be construed to mean **"capable, without toxic effects, of maintaining the serum phosphate level of a subject at a substantially constant level in a subject who has an excess level of serum phosphate."**

IV. CONSTRUCTION OF TERMS OF U.S. PATENT NO. 7,465,465 AND U.S. PATENT NO. 7,381,428

The '428 Patent is a continuation-in-part of the application that issued as the '465 Patent. (That is, the application for the '465 Patent served as the basis for the application for the '428 Patent, with some new matter added.) Accordingly, the '428 Patent builds upon the invention disclosed in its parent patent. Based on the considerable overlap in the disclosures of the two patents, construction of certain terms in both patents is related and will be addressed together here.

A. "Lanthanum carbonate has the formula $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from" ('465 Patent, Claim 3); "Lanthanum carbonate having the formula $La_2(CO_3)_3 \bullet xH_2O$ wherein x has a value from" ('428 Patent, Claims 1 and 7)

Claim Term	Shire's Proposed Construction	Defendants' Proposed Construction
lanthanum carbonate has the formula $La_2(CO_3)_3 \cdot xH_2O$ where x has a value from ('465 Patent)	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from
lanthanum carbonate having the formula $La_2(CO_3)_3 \cdot xH_2O$ wherein x has a value from ('428 Patent)	a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from

The term "lanthanum carbonate has [or 'having'] the formula $La_2(CO_3)_3 \cdot xH_2O$ where [or 'wherein'] x has a value from" in the '465 Patent and '428 Patent should have the same construction as the near-identical term in the '976 Patent, "lanthanum carbonate of the formula $La_2(CO_3)_3 \cdot xH_2O$ wherein x has a value from," discussed above. *See supra* Part III.B; *see also NTP, Inc. v. Research In Motion, Ltd.*, 418 F.3d 1282, 1293 (Fed. Cir. 2005) ("Because NTP's patents all derive from the same parent application and share many common terms, we must interpret the claims consistently across all asserted patents.").

The '465 and '428 Patents expressly incorporate by reference the disclosure of the '976 Patent. JA 0015 ('465 Patent, Col. 4:22-23); JA 0040, 0048 ('428 Patent, Col. 1:44-47, 17:34-37). Materials expressly incorporated by reference in a specification are highly relevant in understanding the claim terms of the patent in which they are referenced. *See, e.g.*, *AquaTex Indus., Inc. v. Techniche Solutions*, 419 F.3d 1374, 1381 (Fed. Cir. 2005) ("Because AquaTex chose to incorporate by reference the teachings of three United States Patents to define the scope of the term "fiberfill," these publications are highly relevant to one of ordinary skill in the art for ascertaining the breadth of the claim term."); *Cook Biotech Inc. v. Acell, Inc.*, 460 F.3d 1365, 1375-78 (Fed. Cir. 2006) (construing a term based in part on specification of prior art patent that was incorporated by reference). Accordingly, Shire's proposed construction discussed above in the context of the '976 Patent should also be adopted in the '465 and '428 Patents. Defendants must agree that these terms have the same meaning as the near-identical term in '976 Patent, having also proposed essentially identical constructions for the terms.

Additionally, as Dr. Myerson explains, a person of ordinary skill in the art would understand the chemical formula appearing in the patents-in-suit to mean the same thing for the same reason—a chemical formula with a "dot x" value for the number of moles of water present is a common way of referring to multiple hydrates of a compound. *See* Myerson Decl. ¶ 53. Nothing in the specification or prosecution history indicates that the applicants intended a specialized meaning for this term.

Defendants' proposed construction, "[t]he lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio from 3 to 8," seeks to change the plain meaning of the chemical formula from a particular crystalline form to refer to an average value across a bulk composition. For reasons discussed above, this

proposed construction is contrary to the ordinary and customary meaning of the term and the intrinsic evidence of the '976 Patent.

The specifications of the '465 Patent and '428 Patent further show that the claimed formula does not refer to the "average water content" of lanthanum carbonate. The specification discloses several preferred embodiments, such as that "x" is "preferably from 4 to 5." JA 0015 ('465 Patent, Col. 4:17-19); JA 0045 ('428 Patent, Col. 11:28-32). In *one* preferred embodiment, "most preferably x has an *average* value of 4." JA 0015 ('465 Patent, Col. 4:19) (emphasis added). By describing "x" as "ha[ving] an average value of 4" in this embodiment, the specification makes clear that "x" is not itself an average value. This further demonstrates that Defendants' attempt to limit the inventions to an average value is improper.

Accordingly, the term "lanthanum carbonate has [or 'having'] the formula $La_2(CO_3)_3 \cdot xH_2O$ wherein x has a value from" should be construed to mean **"a crystalline form of lanthanum carbonate containing x moles of water as part of its crystal structure per mole of lanthanum carbonate."**

B. "lanthanum carbonate is hydrated having a water content of about 4 moles of water" ('465 Patent, Claim 8)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
lanthanum carbonate is hydrated having a water content of about 4 moles of water	lanthanum carbonate present in the tablet has a ratio of approximately 4 moles of water to one mole of lanthanum carbonate	the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio of about 4

Claim 8 is a dependent claim directed to "[t]he chewable lanthanum carbonate pharmaceutical tablet of claim 1," which states that the tablet is made from formulations with particular ingredients in stated amounts. JA 0021 ('465 Patent, Col. 15). Claim 8 recites that in

the chewable tablet, the "lanthanum carbonate is hydrated having a water content of about 4 moles of water." *Id.*

Shire believes that this term has a plain and ordinary meaning and need not be construed. To the extent it must be construed, Shire believes its proposed construction is far clearer than that proposed by Defendants. Defendants confusingly and misleadingly seek to construe "water content" as "*average* water content" and without explanation substitute "composition" (a term not used in the patent) for "tablet," to which the claims refer.

C. "water content" ('428 Patent, Claims 6 and 12)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
water content[6]	ratio of moles of water to one mole of lanthanum carbonate	*Defendants have stated they cannot construe this term*

The issues concerning the construction of "water content" in dependent claims 6 and 12 of the '428 Patent mirror those discussed in the preceding section. Claims 6 and 12 recite, respectively, a method of administering stabilized compositions and a method of stabilizing lanthanum carbonate compositions containing, *inter alia*, lanthanum carbonate with a "water content" approximately equivalent to 4-5 moles of water. JA 0040 ('428 Patent, Col. 18). Shire proposes that the term "water content" take its plain meaning: a "ratio of moles of water to one mole of lanthanum carbonate."

[6] Defendants have declined to propose a construction for "water content." After Shire identified this term, they indicated that they would instead like to construe a broader phrase, "the lanthanum carbonate has a water content approximately equivalent to 4-5 moles of water." This extra verbiage is unnecessary, as Defendants' proposed construction of it shows. Defendants have proposed to construe the phrase to mean "the lanthanum carbonate present in the composition has an average water content equivalent to a water to $La_2(CO_3)_3$ mole ratio of approximately 4-5." In any event, if this long phrase requires construction, Shire proposes the following: "the lanthanum carbonate has a ratio of moles of water to one mole of lanthanum carbonate approximately equivalent to 4-5 moles of water."

D. "substantial decarboxylation"/"stabilizing the lanthanum carbonate against substantial decarboxylation to lanthanum hydroxycarbonate"/"the lanthanum hydroxycarbonate being stabilized against substantial decarboxylation to lanthanum hydroxycarbonate" ('428 Patent, Claims 1 and 7)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
stabilizing the lanthanum carbonate against substantial decarboxylation to lanthanum hydroxycarbonate	retarding the lanthanum carbonate from degrading into lanthanum hydroxycarbonate in an amount sufficient so that a skilled artisan detects lanthanum hydroxycarbonate through visual inspection of an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60º C and 95% relative humidity for at least 7 days	stabilizing the lanthanum carbonate present in the composition such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate is detectable in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after the composition has been exposed to 60º C and 95% relative humidity for at least 7 days, wherein lanthanum hydroxycarbonate is a species characterized by the four peaks identified by "HC" in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days
the lanthanum carbonate being stabilized against substantial decarboxylation to lanthanum hydroxycarbonate	in which the lanthanum carbonate is retarded from degrading into lanthanum hydroxycarbonate in an amount sufficient so that a skilled artisan detects lanthanum hydroxycarbonate through visual inspection of an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60º C and 95% relative humidity for at least 7 days	stabilizing the lanthanum carbonate present in the composition such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate is detectable in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after the composition has been exposed to 60º C and 95% relative humidity for at least 7 days, wherein lanthanum hydroxycarbonate is a species characterized by the four peaks identified by "HC" in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days

The specification of the '428 Patent explains that "lanthanum carbonate has a tendency to degrade via decarboxylation to lanthanum hydroxycarbonate," JA 0041 ('428 Patent, Col. 4:44-

45), through a process accelerated by moisture and heat, JA 0040 ('428 Patent, Col. 1:49-50). There was "a need in the art to prevent this degradation because current regulatory requirements preclude detectable decarboxylation for administration to patients." *Id.* ('428 Patent, Col. 1:50-53). Thus, "[f]ormulations [with lanthanum carbonate] that eliminate or substantially retard degradation are highly preferred." JA 0041 ('428 Patent, Col. 4:58-60). The inventors discovered that the addition of sufficient amounts of monosaccharides or disaccharides significantly slows or prevents the degradation process. JA 0040, 0042 ('428 Patent, Col. 1:53-57, 5:1-6).

Independent claim 1 of the '428 Patent recites "stabilizing the lanthanum carbonate against substantial decarboxylation." JA 0048 ('428 Patent, Col. 17:47-48). Independent claim 7 similarly recites "lanthanum carbonate being stabilized against substantial decarboxylation." JA 0048 ('428 Patent, Col. 18:25-27).

The '428 Patent teaches that "stabilized" means "significantly retard[ing]" the process of decarboxylation or eliminating it entirely. JA 0041 ('428 Patent, Col. 4:55, 4:61-67). Shire's proposed construction accords the term "stabilizing" this clear definition.

The question of how much "decarboxylation" is "substantial" within the meaning of claims 1 and 7 was answered conclusively during prosecution. The Examiner initially rejected claims containing the words "substantial decarboxylation" (but that did not contain the language about observation in an x-ray diffraction pattern after subjecting the samples to specified conditions) on the ground that "[i]t is unclear to the Examiner the metes and bounds of exactly how much decarboxylation is substantial. The Examiner suggests that the limitations of instant claim 25 be incorporated into claim 13." JA 4448 (4/6/06 Office Action at 3); *see also* JA 2669, 2671 (3/16/06 First Preliminary Amendment at 2, 4).

To overcome this rejection, the applicants did what the Examiner suggested, amending the rejected claims to add the following: "wherein the amount of the stabilizer is such that lanthanum hydroxycarbonate is not observed in an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate and the stabilizer after the lanthanum carbonate and the stabilizer have been exposed to 60ºC and 95% relative humidity for 7 days." JA 4666, 4671 (7/5/06 Amendment and Remarks at 4, 9). In response to this amendment, the Examiner withdrew his indefiniteness rejection. JA 4713 (10/30/06 Office Action at 3) ("Applicant amended claim 13 . . . qualifying what substantial decarboxylation means. The Examiner withdraws the rejection.").

Thus, the applicants defined substantial decarboxylation during prosecution by the additional limitation they added to the claim. Shire's proposed construction provides the clear definition of this term from the amendment that overcame the indefiniteness rejection. *See, e.g., Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1298, 1302-03 (Fed. Cir. 2004) (construing claim term according to statements made by Applicants during prosecution to overcome indefiniteness rejection).

Defendants' proposed construction of these terms suffers from several defects. First, Defendants' constructions merely repeat the term "stabilized" or "stabilizing," rather than applying the definition contained in the specification (*i.e.*, that to stabilize means to at least "retard" the degradation process). *See* JA 0041 ('428 Patent, Col. 4:58-60).

Second, Defendants' proposed construction states that stabilizing against substantial decarboxylation entails that decarboxylation not be "detectable," but fails to clarify that preventing substantial decarboxylation is understood in terms of whether decarboxylation is

observable through visual inspection by a skilled artisan, which should be included in these constructions for reasons set forth in the next section.

Third, Defendants improperly attempt to import a limitation from the specification. Defendants propose to define lanthanum hydroxycarbonate as a "species characterized by the four peaks identified by 'HC' in the x-ray powder diffraction pattern appearing in Figure 13 for t = 7 days." But Figure 13 does not purport to define lanthanum hydroxycarbonate. It simply provides x-ray powder diffraction patterns for a specific "stress study" of hydrated lanthanum carbonate mixed with microcrystalline cellulose, in which lanthanum hydroxycarbonate appears. JA 0047 ('428 Patent, Col. 16:32-37). The intrinsic record provides no basis to define lanthanum hydroxycarbonate by the four peaks labeled "HC" in this example, which is but one of many examples provided in the specification. Importing a limitation from the specification is inappropriate. *Voda*, 536 F.3d at 1320; *see also Phillips*, 415 F.3d at 1323.

E. "is not observed in" ('428 Patent, Claims 1 and 7)[7]

Term To Be Construed	Shire's Proposal	Defendants' Proposal
is not observed in	is not detected through visual inspection by a skilled artisan of	*Defendants have stated they cannot construe this term*
the amount of the monosaccharide or disaccharide is such that lanthanum hydroxycarbonate *is not observed in* an x-ray powder diffraction (XRPD) pattern of the lanthanum carbonate composition after it has been exposed to 60 C and 95% relative humidity for at least 7 days	the amount of the monosaccharide or disaccharide contained in a lanthanum carbonate composition is sufficient so that lanthanum hydroxycarbonate is not detected through visual inspection by a skilled artisan of x-ray powder diffraction patterns after the composition has been exposed to 60º C and 95% relative humidity for at least 7 days	the amount of the monosaccharide or disaccharide present in the lanthanum carbonate composition is such that no lanthanum hydroxycarbonate formed by decarboxylation of the lanthanum carbonate present in the composition is detectable in an x-ray powder diffraction (XRPD) pattern of the composition containing lanthanum carbonate and one or more monosaccharides or disaccharides after the composition has been exposed to 60º C and 95% relative humidity for at least 7 days

The '428 Patent teaches that the experimental technique of x-ray powder diffraction may be used to detect the presence of lanthanum hydroxycarbonate. *See, e.g.*, JA 0042 ('428 Patent, Col. 5:18-21); Myerson Decl. ¶ 55.

The plain meaning of the term "observed" to a person of ordinary skill in the art implies a visual inspection of the x-ray powder diffraction pattern obtained from a test, comparing that pattern to a reference pattern. *See* Myerson Decl. ¶¶ 56-57. The Figures of the '428 Patent further suggest that the "detection" of lanthanum hydroxycarbonate is by visual inspection, as they show the presence of lanthanum hydroxycarbonate observable in this manner and the

[7] The parties were unable to agree on the appropriate claim term to construe, leading to overlapping claim terms. Shire submits that it is apparent from the proposed constructions that the only term requiring interpretation is "is not observed in."

specification does not discuss other manners of detecting lanthanum hydroxycarbonate. *Compare* JA 0032, 0047 ('428 Patent, Fig. 8, Col. 15:48-56) (degradation "detected" after one day of a stress study); *with* JA 0035-36, 0038, 0047 ('428 Patent, Figs. 11, 12, 14, Col. 16:17-26, 43:54) (Examples 6.5.2.9, 6.5.2.11) (no degradation visible to the naked eye for experiments in which, according to the specification, degradation was not "detectable"). And this understanding is further confirmed by Plaintiffs' expert, Dr. Myerson. As explained more fully in his declaration, a person of ordinary skill in the art would determine whether characteristic peaks of lanthanum hydroxycarbonate are present by a visual inspection of the x-ray powder diffraction pattern obtained from the test. Myerson Decl. ¶¶ 56-58.

Defendants' proposed construction fails to clarify how detection is performed and contains redundancies ("of the monosaccharide or disaccharide present in the lanthanum carbonate composition is such … of the composition containing lanthanum carbonate and one or more monosaccharides or disaccharides") that cannot be helpful to the Court.

Accordingly, "is not observed in" should be construed to mean **"is not detected through visual inspection by a skilled artisan of."**

F. "therapeutically effective amount" and "amount effective to treat hyperphosphatemia" ('428 Patent, Claim 1)

Term To Be Construed	Shire's Proposal	Defendants' Proposal
therapeutically effective amount	amount or dose sufficient (i) to detectably decrease the serum phosphate levels of a subject or (ii) at a minimum, to keep the serum phosphate levels of a subject substantially constant	wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphataemia
amount effective to treat hyperphosphatemia	amount or dose of lanthanum carbonate sufficient (i) to detectably decrease the serum phosphate levels of a subject or (ii) at a minimum, to keep the serum phosphate levels of a subject substantially constant	wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphataemia.

Shire proposes that the term "therapeutically effective amount" be construed as it is expressly defined in the specification of the '428 Patent. *See* JA 0041 ('428 Patent, Col. 4:1-6). "When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term." *Sinorgchem Co.*, 511 F.3d at 1138. Defendants disregard this fundamental canon of claim construction. Indeed, Defendants' proposed alternative construction of the term – which parallels their unsupportable proposed constructions for similar terms in the '976 Patent – simply underscores the extent to which they have departed from governing claim construction principles in favor of constructions of convenience.

As to "amount effective to treat hyperphosphatemia," the prosecution history demonstrates that it has the same meaning as therapeutically effective amount. The specification equates "pharmaceutically effective amount" with "therapeutically effective amount." JA 0041 ('428 Patent, Col. 4:1-6). In an amendment filed before the Patent Office took any action on the application, the applicants substituted "an amount effective to treat hyperphosphatemia" for "a

pharmaceutically effective amount of" in what became claim 1. *See* JA 2669 (3/16/06 Amendment and Remarks at 2). Applicants did not refer to this amendment in the accompanying remarks, and there is no indication that they intended to make any substantive change through this substitution. *See* JA 2672 ("By this amendment, no new matter has been added to this application."). Accordingly, the term "amount effective to treat hyperphosphatemia" should have the same meaning as "therapeutically effective amount." Defendants must agree, as they have proposed the same construction for both terms.

Shire's proposed construction of "amount effective to treat hyperphosphatemia" is also consistent with all the other intrinsic evidence. The term "treat" is defined in the specification to mean "the prevention, reduction, amelioration, partial or complete alleviation, or cure of hyperphosphatemia, chronic kidney disease (CKD), severe bone problems, soft tissue calcification, secondary hyperparathyroidism, or other as yet undiscovered conditions requiring control of phosphate absorption." JA 0041 ('428 Patent, Col. 3:16-22). This definition makes clear that the *sine qua non* of "treatment" is controlling phosphate absorption, which in the context of hyperphosphatemia can involve either reducing hyperphosphatemia (*i.e.*, decreasing elevated serum phosphate levels) or at a minimum its "prevention" (*i.e.*, keeping phosphate levels substantially constant). *See generally* Scheel Decl. ¶¶ 36-37.

Defendants ask that these terms be construed to mean "wherein the amount of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition is effective to treat hyperphosphatemia." This proposed construction gratuitously inserts a limitation ("of $La_2(CO_3)_3 \cdot xH_2O$ present in the composition") – the same limitation they have sought to add time and again to their constructions, *see supra* Parts III.A, III.C, III.D – and ignores the definitions contained in the specification.

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